

CLAIMS

We claim:

1. A method for preparing a microarray of frozen tissue and/or cell samples comprising the
5 steps of:
 - (a) providing a microarray block comprising a plurality of donor tissue and/or cell samples embedded in a block of frozen embedding material, each of said donor samples having a known location in said block;
 - (b) sectioning said block to generate a section comprising portions of said plurality of donor samples, each portion of each donor sample at a different sublocation in the section at coordinates corresponding to coordinates of the donor sample in the microarray block from which each portion was obtained; and
 - (c) placing said section on a substrate such that said portions at different sublocations are stably associated with said substrate, thereby generating said microarray.
- 10 2. The method according to claim 1, wherein said microarray block comprises about 10 to about 1200 samples.
- 15 3. The method according to claim 1, wherein at least one of said donor samples is a tissue sample.
- 20 4. The method according to claim 1, wherein at least one of said donor samples is a cell sample.
- 25 5. The method according to claim 1, further comprising generating said microarray block, said generating comprising the steps of:
 - (d) obtaining a donor sample from a donor block comprising a tissue or cell sample embedded in frozen embedding material;
 - (e) providing a recipient block comprising a frozen embedding material;
 - (f) generating a hole in said recipient block sized to receive said donor sample; and

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(g) filling said hole with said donor sample.

6. The method according to claim 5, further comprising repeating steps (d) through (g) multiple times.
7. The method according to claim 5, wherein said obtaining is performed by using a coring needle comprising a cutting edge and wall defining a lumen to core a donor sample.
8. The method according to claim 6 or 7, wherein said core is in the shape of a cylinder.
9. The method according to claim 8, wherein said core is about 0.3 mm in diameter.
10. The method according to claim 8, wherein said core is about 0.6 mm in diameter.
11. The method according to claim 8, wherein said core is greater than about 0.6 mm.
12. A method of generating a microarray block, comprising the steps of:
 - (a) obtaining a donor sample from a donor block comprising a tissue or cell sample embedded in frozen embedding material;
 - (b) providing a recipient block comprising a frozen embedding material,
 - (c) generating a hole in said recipient block sized to receive said donor sample; and
 - (d) filling said hole with said donor sample.
13. The method according to claim 12, further comprising repeating steps (a) to (d) multiple times.
14. The method according to claim 6 or 13, wherein said method is automated.
- 20 15. The method according to claim 14, wherein information relating to the location of each donor sample in said recipient block is stored in a database.
16. A microarray block comprising a plurality of donor tissue and/or cell samples embedded in a block of frozen embedding material, each of said donor samples having a known location in said block.
- 25 17. The microarray block according to claim 16, wherein at least one sample is from a human.

18. The microarray block according to claim 16, wherein at least one sample is from an individual having a disease.
19. The microarray block according to claim 18, wherein said disease is a progressive disease, and said block comprises a plurality of samples representing different stages in the progression of the disease.
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20. The microarray block according to claim 18, wherein said disease is cancer.
21. The microarray block according to claim 18, wherein said disease is a neurodegenerative disease.
22. The microarray block according to claim 18, wherein said disease is a neuropsychiatric disease.
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23. The microarray block according to claim 16, wherein said block comprises both tissue samples and cell samples.
24. The microarray block according to claim 16, wherein said block comprises a plurality of different types of tissue samples from the same individual.
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25. The microarray block according to claim 24, comprising at least 5 different types of tissues from the same individual.
26. The microarray block according to claim 24, comprising at least 10 different types of tissues from the same individual.
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27. The microarray block according to claim 24, further comprising a cell sample from said individual.
28. The microarray block according to claim 27, wherein said cell sample is from a bodily fluid from said individual.
29. The microarray block according to claim 16, wherein at least one sample is from a fetus.

30. The microarray block according to claim 16, wherein at least one sample is from a non-human animal.
31. The microarray block according to claim 30, wherein said non-human animal comprises at least one cell comprising an exogenous nucleic acid.
- 5 32. The microarray block according to claim 30, wherein said non-human animal is a model of a disease.
33. The microarray block according to claim 32, wherein said non-human animal has been treated with a therapy for treating said disease.
34. The microarray block according to claim 16, wherein at least one donor sample is from a plant.
- 10 35. A microarray comprising a substrate on which a plurality of frozen tissue or frozen cell samples are disposed at a plurality of known sublocations made according to the method of claim 1.
36. The microarray according to claim 35, wherein at least one sample is from a human.
- 15 37. The microarray according to claim 35, wherein at least one sample is from an individual having a disease.
38. The microarray according to claim 37, wherein said disease is a progressive disease, and said microarray comprises a plurality of samples representing different stages in the progression of the disease.
- 20 39. The microarray according to claim 37, wherein said disease is cancer.
40. The microarray according to claim 37, wherein said disease is a neurodegenerative disease.
41. The microarray according to claim 37, wherein said disease is a neuropsychiatric disease.

42. The microarray according to claim 35, comprising both tissue samples and cell samples.
43. The microarray according to claim 35, comprising a plurality of different types of tissue samples from the same individual.
- 5 44. The microarray according to claim 36, comprising at least 5 different tissue types from the same individual.
45. The microarray according to claim 35, comprising at least 10 different tissue types from the same individual.
46. The microarray according to claim 35, further comprising a cell sample from said individual.
- 10 47. The microarray according to claim 46, wherein said cell sample is from a bodily fluid from said individual.
48. The microarray according to claim 35, wherein at least one sample is from a fetus.
49. The microarray according to claim 35, wherein at least one sample is from a non-human animal.
50. The microarray according to claim 49, wherein said non-human animal comprises at least one cell comprising an exogenous nucleic acid.
51. The microarray according to claim 50, wherein said non-human animal is a model of a disease.
- 20 52. The microarray according to claim 51, wherein said non-human animal has been treated with a therapy for treating said disease.
53. The microarray according to claim 16, wherein at least one donor sample is from a plant.
54. A method of evaluating a tissue or cell sample, comprising:

providing the microarray of claim 35;
contacting said microarray with a molecular probe; and
determining which sublocations of said microarray react with said molecular probe.

- 5 55. The method according to claim 54, wherein said evaluating comprises correlating reactivity of said probe with one or more characteristics of the individual from which a sample at a reacted sublocation was obtained.
56. The method according to claim 55, wherein said one or more characteristics comprises the presence of a disease.
- 10 57. The method according to claim 56, wherein said correlating identifies the molecular probe as a candidate diagnostic probe for detecting said disease.
58. The method according to claim 56, wherein at least one of said samples from said microarray is from an individual treated with a drug for treating a disease.
59. The method according to claim 56, wherein said individual treated with said drug has the disease.
60. The method according to claim 58 or 59, further comprising comparing the reactivity of said at least one of said samples to a sample from an individual not treated with said drug.
61. The method according to claim 60, wherein said individual not treated with said drug does not have said disease.
- 20 62. The method according to claim 56, wherein said disease is cancer.
63. A method for identifying the specificity of a molecular probe comprising:
providing the microarray of claim 35, wherein said microarray comprises a plurality of different types of tissue samples from the same individual;
reacting said microarray with said molecular probe; and
determining which of said tissue samples react with said molecular probe.

64. The method according to claim 63, wherein said plurality comprises at least about 5 different tissue samples.
65. The method according to claim 63, wherein said microarray further comprises at least one cell sample from a bodily fluid of said individual.
- 5 66. A method for identifying a candidate diagnostic probe, said method comprising:
providing a molecular probe corresponding to a differentially expressed sequence;
reacting said molecular probe with a plurality of microarrays according to claim 1, said plurality comprising samples from individuals having a trait and from individuals not having said trait;
determining the presence or absence of a correlation between the reactivity of said probe and said trait; wherein the presence of a correlation identifies said probe as a diagnostic probe.
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67. The method according to claim 66, wherein said differentially expressed sequence is identified by performing electronic subtraction of a sequence database.
- 15 68. The method according to claim 67, wherein said differentially expressed sequence is identified by:
providing a nucleic acid microarray comprising a plurality of known sequences;
contacting said nucleic acid microarray with first nucleic acids from an individual having a trait, said first nucleic acids labeled with a first label;
20 contacting said nucleic acid microarray with second nucleic acids from an individual not having said trait, said second nucleic acids having a second label; and
identifying sequences in said plurality of known sequences which do not hybridize to both said first and second label.
- 25 69. The method according to claim 66, wherein said differentially expressed sequence is identified by:
providing a first nucleic acid microarray comprising a plurality of known sequences and a second nucleic acid microarray, said second nucleic acid microarray

comprising sequences identical to said plurality of known sequences on said first microarray;

contacting said first nucleic acid microarray with labeled nucleic acids from an individual having said trait;

5 contacting said second nucleic acid microarray with labeled nucleic acids from an individual not having said trait; and

identifying sequences which differentially hybridize in said first and second microarray.

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